Quick guide

Fas

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What is it? Fas is a cell-surface receptor, and one of the main triggers of death in cells of the immune system. A cell bearing Fas can be set on a cell death (apoptosis) pathway when the ligand FasL binds to Fas.

Also known as… Apo-1 (in Germany); CD95 (by a few immunologists).

It came to prominence… in 1995 and 1996, when a signaling pathway downstream of Fas was described, providing the first molecularly defined link between a cell-surface receptor and the core cell death machinery (see Figure).

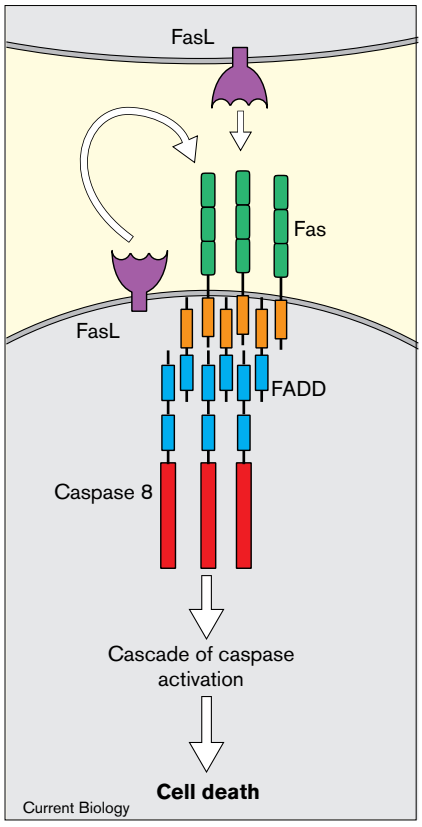
Not to be confused with… Ras, a small GTPase, or Fos, a transcription factor.

Where is it found? Fas is expressed at various levels in a wide range of cell types. But a cell carrying Fas isn't necessarily condemned to death; fortunately, FasL expression is very restricted and even once the signalling pathway has been triggered, it can be blocked downstream of Fas.

Its known functions are… in the elimination of activated lymphocytes at the end of an immune response; as part of the mechanism by which immunoprivileged sites such as the eye and the testis evade the immune system.

Why all the fuss about Fas? Fas seems to be essential for killing off the immune response before it goes out of control. Mice bearing spontaneous loss-of-function mutations in Fas and FasL have enlarged spleens and lymph glands, and some mouse strains have a form of autoimmunity, due to a defect in the elimination of activated lymphocytes. Mutations in Fas have also been described in children with autoimmune lymphoproliferative syndrome (ALPS). Fas is now also thought to be involved in cell death outside the immune system, especially in cancer and other non-infectious diseases.

Who are its known associates? The intracellular 'death domain' of Fas binds to the FADD adaptor protein, which in turn recruits caspase-8 (see Figure), thereby initiating the proteolytic cascade of events characteristic of apoptosis. Fas also interacts with Daxx, which sensitizes cells to death, and with FAP-1, a protein tyrosine phosphatase that was reported some time ago to inhibit cell death signaling but which is now rather out of fashion.



The Fas signalling pathway. Assembly of the Fas oligomer by FasL – expressed on another cell or produced by the same cell (as in the elimination of activated lymphocytes) – triggers the cell death (apoptosis) pathway. Cysteine-rich repeat, green; death domain, orange; death effector domain, blue, caspase domain, red.

Does Fas have any relatives? Fas is related to tumour necrosis factor receptor 1 (TNFR1), by virtue of its extracellular cysteine-rich repeats, and is therefore classified as a member of the TNFR family, which includes other death receptors, such as DR3, DR4 and DR5, as well as some cell-surface immunoreceptors.

Does it have commercial potential? Yes. Increased Fas activity is thought to be involved in fulminant hepatitis (a severe form of the disease) and in thyroiditis, in the excess T-cell death that occurs in AIDS, and in some cases of tissue rejection following transplantation. Decreased Fas signalling has been associated with the lack of death of certain types of tumour cell; acquired FasL expression is another way for tumour cells to evade the immune system. So, there is interest in interfering with Fas-induced cell death, although this would have to be done selectively; injection of anti-Fas antibodies kills mice within a few hours.

Where can I find out more?

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